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Systemic Treatment of Psoriasis in Children

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Abstract

Childhood psoriasis has a significant impact on the child´s quality of life and those who cannot be managed with topical treatment should be considered for systemic treatment. The majority of systemic therapies used for childhood psoriasis are off-label drug therapies. Evidence-based studies on systemic treatment of childhood psoriasis are scarce, and treatment algorithms are generally based on low-level evidence. A literature search was performed and updated to October 2015 to obtain an up to date overview of relevant systemic treatment in childhood psoriasis. Methotrexate is the conventional first-line of systemic treatment, but the level of evidence for its use is low. Etanercept is FDA approved for psoriasis vulgaris in children, has a documented efficacy and a good safety profile, and is currently the drug for which most evidence for the use in children has been accumulated. Adalimumab and ustekinumab have both recently completed large double-blinded controlled trials testing in childhood psoriasis and both have recently been approved for psoriasis vulgaris in children. Thus a wider range of approved systemic treatment options is becoming available.

Keywords: Psoriasis; Skin disease; Childhood; Paediatric; Biologics; Methotrexate

Introduction

Psoriasis is a chronic inflammatory skin disease affecting approximately 1-3% of the population and recent years have seen a rising incidence of childhood psoriasis [1]. Early onset during infancy, childhood or adolescence has a significant impact on the child´s quality of life, and those who cannot be managed with topical treatment should be considered for systemic treatment. Most current systemic therapies used to treat childhood psoriasis are off-label drug therapies that have not been approved for use in this age group.

Level of evidence (LOE)	Definition	Systemic treatment of psoriasis in children
1a	Systematic review of Randomized controlled trials (RCT)	-
1b	Individual RCT	Etanercept/placebo
		Adalimumab/mtx
		Ustekinumab/placebo
2a	Systematic review of cohort studies	-
2b	Individual cohort study (including low quality RCT)	-
3a	Systematic review of case- control studies	-
3b	Individual case–control study	-
4	Case series	Retinoids, Cyclosporine, Fumaric acid esters
5	Case reports, expert opinion	Infliximab

Table 1: Level of evidence (LOE). Adjusted from Oxford center for evidence-based medicine levels of evidence. The treatment options applied concordantly to their individual LOE.

Current psoriatic guidelines or consensus articles only sparsely address treatment in children [2-4]. Furthermore, in 2014 a multicentre audit performed in the UK indicated considerable variation in the management of children with psoriasis [5]. Thus, a guideline for the treatment of childhood psoriasis that rests on high level of evidence is strongly needed. Pending the provision of such evidence, the present review aims to present an updated overview of relevant systemic treatment options available for treating childhood psoriasis. In the following, each treatment will be described

individually, and the level of evidence (LOE) will be evaluated (Table 1).

Methods

A literature search was performed and updated to October 2015 in PubMed using "psoriasis"; the drug of choice "methotrexate", "cyclosporine", "retinoids", "fumaric acid esters", "etanercept", "adalimumab", "infliximab", "ustekinumab"; and "children" or synonyms such as "adolescent", "childhood" or "paediatric" as keywords. The search revealed 620 articles, which were to be screened for inclusion. All studies from single-case reports to randomised controlled trials were included. Furthermore, both studies using the drug as monotherapy and studies using combination therapy were included. In addition, both treatments of psoriasis vulgaris and pustular or erythrodermic psoriasis were considered relevant. The population age included was limited to age<18 years, and only English-language papers were included. The included studies are shortly summarised in Table 2.

Study type	No. of patients	Treatment	Effect	Author
Case report	1	MTX	almost complete remission	Dogra et al. (2004)
Case report	1	MTX	remarkable clearance	Dogra et al. (2005)
Case report	1	MTX	full skin recovery	Teran et al. (2010)
Case report	1	MTX	responded well	Björksten et al. (1975)
Case report	1	MTX	marked improvement	Kalla et al. (1996)
Case report	2	MTX	significant improvement	Garg et al. (2011)
Case report	1	MTX	switched from acitretin to mtx	Popadic et al. (2014)
Retrospective Case series	13	MTX	11 achived clearance with small residual plaques	Collin et al. (2008)
Retrospective Case series	24	MTX	22 patients reached PASI 75; 2 achived PASI 50-75	Kaur et al. (2008)
Retrospective Case series	7	MTX	7 achived >75% clearance	Kumar et al. (1994)
Retrospective Case series	4	MTX	4 had good responses	Juanqin et al. (1998)
Retrospective Case series	25	MTX	40% achived PASI 75 at week 36	Geel et al. (2015)
Case report	1	Cyclosporine	marked response	Nakamura et al. (2009)
Case report	1	Cyclosporine	resolved completely	Xiao et al. (2007)
Case report	1	Cyclosporine	1 successfully managed	Kim et al. (2006)
Case report	1	Cyclosporine	free of psoriasis	Alli et al. (1998)
Case report	1	Cyclosporine	PASI 40.7 to 4.8	Wollina et al. (2001)
Case series	4	Cyclosporine	2 achived remission	Popadic et al. (2014)
Case series	2	Cyclosporine	Consistent clearing	Campione et al. (2014)
Case series	6	Cyclosporine	3 achived complete remission, 3 responded on dose increase	Pereira et al. (2006)
Case series	4	Cyclosporine	4 unsatisfactory results	Mahé et al. (2001)
Case series	3	Cyclosporine	3 achived clearance	Kilic et al. (2001)
Case series	3	Cyclosporine	3 effective	Perrett et al. (2003)
Case series	17	Retinoids	good response	Popadic et al. (2014)
Retrospective Case series	10	Retinoids	10 improved (7 completely)	Rosinska et al. (1988)
Retrospective Case series	11	Retinoids	7 excellent response, 4 moderat-good response	Juanqin et al. (1998)
Case report	1	Retinoids	improved	Umezawa et al. (2012)

Case report	1	Retinoids	complete clearance	Van der Kerkhof et al. (1985)
Case report	1	Retinoids	cleared	Kopp et al. (2004)
Case report	1	Retinoids	complete remission	Salleras et al. (1995)
Case report	1	Retinoids	partial remission	Judge et al. (1993)
Case report	1	Retinoids	marked improvement	Chao et al. (2009)
Case report	1	Retinoids	complete remission, then relapse and then improvement	Ergin et al. (2008)
Case report	1	Retinoids	minimal disease activity	Liao et al. (2002)
Case report	1	Retinoids	good results but relapse	Mazzatenta et al. (2005)
Case series	2	Retinoids	marked improvement	Shelnitz et al. (1987)
Case series	2	Retinoids	2 excellent response	Van der Rhee et al. (1980)
Case series	7	Retinoids	3 disease free, 4 lost	De Oliveira et al. (2010)
Case report	1	Retinoids	excellent outcome	A-Shobaili et al. (2007)
Retro-spective Case series	14	FAE	5 complete clearance, 1 good response, 3 partiel response, 5 non-response	Balak et al. (2013)
Retro-spective Case series	6	FAE	6 achived PASI 75-100	Steinz et al. (2014)
Case report	1	FAE	succesfull treatment	Gerdes et al. (2011)
Retro-spective Case series	14	FAE	9 achieved improvement in PASI	Geel et al. (2015)
Randomised controlled trial	211	Etanercept placebo	eg. After 12weeks: PASI 75:57% compared to 11% in placebo group	Paller et al. (2008)
extended open-label/double blinded	138	Etanercept	eg. After 12 weeks: 70-85% maintained or regainded PASI 75	Siegfried et al. (2010)
extented open-label	140	Etanercept	47% achieved clear/almost clear	Paller et al. (2010)
retrospective Case series	9	Etanercept	3 cleared, 4 much improved, 2 equivocal	Hawrot et al. (2006)
Case series	4	Etanercept	4 achived reduced PASI between 7-25.8	Papoutsaki et al. (2005)
Case series	10	Etanercept	10 clear/almost clear	Kress et al. (2006)
Case report	1	Etanercept	PASI 37 to 1.2 after 12 weeks	Fabrizi et al. (2007)
Case report	1	Etanercept	sustained improvement	Safa et al. (2007)
Case report	1	Etanercept	sustained improvement	Floristan et al. (2011)
Case report	1	Etanercept	excellent response	Fraga et al. (2011)
Case report	1	Etanercept	significant response	Fialová et al. (2014)
Case report	1	Etanercept	no response, switched to infliximab	Farnsworth et al. (2005)
Case report	1	Etanercept	slow improvement	Pereira et al. (2006)
Case report	1	Adalimumab	near total resolution	Callen et al. (2005)
Randomised controlled trial	114	Adalimumab/MTX	Adalimumab:57,9% achieved PASI 75; MTX: 32,4% achived PASI 75	ClinicalTrials (2015)
Case report	1	Adalimumab	complete resolution	Alvarez et al. (2011)
Case report	1	Infliximab	marked clearing	Farnsworth et al. (2005)

Case report	1	Infliximab	remission in 10months, then switched to etanercept	Pereira et al. (2006)
Case report	1	Infliximab	improved	Rott et al. (2007)
Case report	1	Infliximab	Complete remission	Skrabl-Baumgartner et al. (2015)
Case report	1	Infliximab	significant improvement	Menter et al. (2004)
Case report	1	Ustekinumab	1 year: PASI 100	Fotiadou et al. (2011)
Case report	1	Ustekinumab	8 weeks: PASI 100	Dixit et al. (2013)
Case report	1	Ustekinumab	8 weeks: PASI 100	AbuHilal et al. (2015)
Randomised controlled trial	110	Ustekinumab Placebo	12 weeks:	Landells et al. (2015)
			>67% achived PGA 0/1	
			>78% achived PASI 75	
			>54% achived PASI 100	

Table 2: Summary of included and published studies.

Results

Methotrexate (mtx)

As a folic acid antagonist that irreversibly binds the dihydrofolate reductase, mtx inhibits RNA and DNA synthesis resulting in cell cycle arrest which curbs the rapid cell proliferation seen in psoriasis. Furthermore the cytokine production of TNF-α, IL-6 and IL-8 is reduced. This provides the rationale for using mtx when treating psoriasis and other well-known diseases such as inflammatory bowel diseases, juvenile arthritis and certain cancers. All these diseases are seen in children and mtx is widely used as the systemic drug of choice, even though the use of mtx has not been approved in this agegroup [6].

The literature search produced 13 studies on the treatment of childhood psoriasis with mtx. The study designs were five single-case reports [7-11], one double-case report [12], and one single-case report in a retrospective study of 18 children mostly treated with acitretin [13]. Most recently published study is a prospective, observational cohort study enrolling 25 children with moderate to severe plaque-type psoriasis treated with mtx and followed for up to 48 weeks. They concluded a positive clinical effect and reasonable safety profile of mtx [14]. The last four studies were all retrospectively reviewed Case series [15-18]. These studies presented 81 paediatric psoriasis patients treated with mtx with overall good response. In a review of 13 cases of childhood psoriasis 11 responded with clearance of psoriasis. Oral methotrexate was commenced at 0.03–0.24 mg/kg/week and increased to 0.1–0.41 mg/kg/week according to response. The duration of treatment was 6 to 267 weeks. Treatment-free intervals between 9 to 22 months were reported without relapse. Two patients stopped treatment due to elevation of liver enzymes [15]. The authors of all other publications administered mtx dosages between 0.2 and 0.4 mg/kg/week. In a review, 24 patients received mtx treatment for 2 to 16 months and 22 patients reached a psoriasis area and severity index (PASI) of 75, whereas the remaining patients reached a PASI of 50-75 [16]. A Case series of seven patients showed control of disease classified as more than 75% clearance of lesions and minimal scaling and erythema in all patients after 6 to 10 weeks. Total treatment duration was 31.2 to 46.4 weeks [17]. In the remaining cases (n=11) in which psoriasis was treated with mtx, a marked improvement to complete remission was reached after varying lengths (weeks) of treatment [7-12,18]. Mild to severe nausea and vomiting were the most frequently reported adverse events; they were seen in approximately 45% of patients [15-17]. In one study, a transient minor elevation of liver enzymes was seen in 60% of the patients, in one case leading to discontinuation of treatment [15]. One case report and one Case series failed to describe side effects [11,18]. Based on the available literature, mtx is an effective treatment option in moderate to severe childhood psoriasis. A double-blinded, controlled trial comparing adalimumab with mtx was completed in December 2014 which provides mtx with LOE at level 1b. However adalimumab demonstrated significantly improvement in PASI 75 compared with mtx [19].

Cyclosporine

By the intracellular binding of cyclophilin, cyclosporine inhibits calcineurin resulting in decreased production of several inflammatory cytokines. The side effects are mainly renal, causing elevated blood pressure and renal insufficiency [6]. The literature search produced 11 studies on the treatment of childhood psoriasis with cyclosporine, either as combination therapy or as monotherapy. Five Case series [13,20-23], five case reports [24-28] and a double case report [29] were identified.

One Case series presented six children aged between 11 months and 13 years who were treated with cyclosporine. They were all unresponsive to other treatments. Doses ranged from 2 to 4 mg/kg/day; treatment periods varied from 8 to 105 weeks. The treatment was tapered gradually after improvement of the skin. Topical adjuvant therapy was used in all children and systemic acitretin was used in three patients for short periods. Improvement of skin lesions was achieved after between 4 and 30 weeks of treatment. Complete remission was seen in three of the six children. Relapse of lesions occurred in the other children during dose reduction, but they later responded to an increase in dosing. The treatment was found to be well tolerated and to have no significant side effects [20]. Several other cases presented similar, promising outcomes on doses typically between 1- 5.4 mg/kg/day and reported satisfactory responses after

2-16 weeks, mostly with minimal adverse effects [22-29]. Although the majority of publications describing the use of cyclosporine in childhood psoriasis were favourable, one article presented four cases who all failed to achieve sufficient response [21]. Furthermore, four cases reported in a retrospective study of 18 children were all treated with acitretin or prednisolone in combination with cyclosporine at doses of <5 mg/kg/day and only two gained remission [13]. The LOE is judged as 4 for the use of cyclosporine in childhood psoriasis, and no double-blinded, placebo-controlled trials exist.

Retinoids

Retinoids, such as acitretin and isotretinoin, inhibit keratinocyte proliferation, promote keratinocyte differentiation and reduce inflammation. Acitretin is the active metabolite of etretinate [6]. The literature search produced numerous studies concerning the treatment of childhood psoriasis with retinoids, either as monotherapy or in combination with cyclosporine or phototherapy. A recent retrospective study published in 2014 presented 18 children with pustular psoriasis. Seventeen children were treated with acitretin at doses ranging from 0.5-1 mg/kg/day. Three patients were treated with acitretin in combination with cyclosporine. Follow-up was 2-19 years and three patients were lost to follow-up. The authors concluded that retinoids are a good and safe treatment option for childhood psoriasis [13]. Another retrospective study reviewed ten patients treated with etretinate at an initial dose of 1mg/kg/day with treatment duration of 3 week to more than 12 months. All patients improved and seven achieved complete clearance [30]. One other retrospective study evaluated 30 children, 2-12 years old, with generalised pustular psoriasis (GPP). Eleven were treated with etretinate 0.2-1mg/kg/day as monotherapy or in combination with prednisolone or erythromycin. Seven gained excellent response and the remaining four achieved good to moderate response [18].

All other publications portrayed single cases or Case series using etretinate or acitretin with overall good results and tolerability, even in infants [31-42]. One case presented a 16-year-old girl with GPP successfully treated with isotretinoin 40 mg/day [43]. Even though most publications described few and tolerable side effects such as cheilitis, skin fragility and hair loss, more serious side effects are known. Retinoids, for example, are teratogenic and can cause significant bone changes in children [30,37,41,44,45]. The existing studies concerning retinoids in the treatment of psoriasis in children is evaluated as LOE 4, and no double-blinded, placebo-controlled trials have been conducted.

Fumaric acid esters (FAE)

Fumarates have been studied and used in the treatment of psoriasis for decades, but their mechanisms of action of fumarates remain unknown. A retrospective Case series from 2013 presented 14 patients with psoriasis (age<18 years) treated with FAE. The median duration of FAE treatment was 10 months, and the median maintenance dosage per day was 360 mg (range 240-600 mg). Five patients achieved complete clearance of their psoriasis, one patient had a good improvement, three patients had partial response, and five patients were non-responders. FAE treatment was generally well tolerated, although two patients discontinued FAE, one with severe diarrhoea and one with flushing [46]. Another recently published retrospective study from 2014 presented six patients aged 6-17 years treated with FAE. The mean duration of treatment was 17.8 months. PASI response and reduction in body surface area (BSA) involvement were determined after 12 weeks. All patients showed improvement in skin condition, two achieving a PASI of 75, one a PASI of 90 and three a PASI of 100. Proteinuria was encountered in one patient, and two patients suffered from gastrointestinal discomfort. Treatment was discontinued due to remission in two patients. Treatment was initiated with one tablet of Fumaderm® (a mixture of dimethyl fumarate and ethylhydrogen fumarate salts with registration for treatment of moderate to severe psoriasis in Germany since 1994) a day with a weekly dose increase as recommended for adults for 3 weeks. Treatment was then continued with a weekly dose escalation of one tablet as long as tolerated and necessary to achieve a treatment success or until a maximum of six tablets per day (720 mg) [47]. Similarly, a case report described the successful long-term treatment of a case of severe psoriasis in an 11-year-old boy [48]. Most recent a prospective Case series of 14 patients with plaque-type psoriasis in the age from 8-17 was published. Daily dose was 180-1200 mg and nine patients had improvement in PASI score [49]. The authors of the reviewed papers all conclude that FAE is an effective and safe treatment for children with psoriasis. However, no double-blinded, placebo-controlled trials have been conducted, and the LOE is evaluated as 4 for the use of FAE in childhood psoriasis.

Etanercept

As a receptor fusion protein targeting TNF-α, etanercept blocks the interaction of TNF-α with its receptor. Etanercept is approved for psoriasis vulgaris in children from the age of 6 years, and it is the biologic agent for which most evidence for the use in children has been accumulated [6,50].

The literature search produced several studies concerning the treatment of childhood psoriasis where etanercept is used as monotherapy or in combination with adjuvant topical or systemic therapy or phototherapy. Of most relevance is a phase III placebo-controlled, randomised and double-blinded trial which presents 211 children aged 4-17 years with psoriasis vulgaris treated once weekly with etanercept 0.8 mg/kg or placebo over 48 weeks. At week 12, 27% of the children receiving etanercept had achieved a PASI response of 90 compared with 7% in the placebo-treated group. Furthermore, a PASI response of 75 was achieved by 57% of etanercept-treated patients compared with 11% of placebo-treated patients [51]. Overall, most of the side effects described in the study consisted of mild and predominantly local injection site reactions. Three patients experienced other adverse events; one case of pneumonia, one case of recurrent gastroenteritis and dehydration and one patient had an ovarian cyst. Etanercept was concluded to be well tolerated in an extended publication performed on the same data described above [52]. In a single-case report, lichen planopilaris was reported as an adverse event in a child treated for psoriasis with etanercept [53].

An open-label extension study evaluated 140 patients who completed 96 weeks of treatment. In 47% of these children, their psoriasis cleared or almost cleared.

Another extension study addressed the issue of intermittent therapy that occurs for a variety of reasons such as disease remission, concurrent diseases and surgery; and in some counties interruption is due to loss of insurance coverage. The potential risks of intermittent therapy include relapse, rebound or failure to regain efficacy. The study showed that intermittent use of etanercept in children with psoriasis was well tolerated. A PASI of 75 for up to 12 weeks was maintained in more than half of the patients, and efficacy was regained within 4 to 8 weeks in one third of patients retreated with etanercept [54].

Furthermore, the response to etanercept was analysed for subgroups of age, gender, BSA, PASI, Physician's Global Assessment (PGA), disease duration and previous therapy; and the results were found to be similar across these groups [55]. Also the impact of etanercept on the quality of life was evaluated, and it showed a clinically and statistically meaningful impact [56]. Additionally, several case reports and Case series demonstrate the efficacy of etanercept for treatment of various types of psoriasis in children, such as plaque type, erythrodermic, generalised pustular and palmoplantar psoriasis [57-64].

However, data on the failure of etanercept in childhood psoriasis also exist. One case of childhood psoriasis of plaque type achieved no improvement after 8 months of treatment, and treatment was switched to infliximab with good response [65]. Likewise, a case not re-responding to infliximab and then switched to etanercept has been described [66]. The long-term safety of etanercept used in children is mostly described based on data derived from rheumatic diseases such as juvenile idiopathic arthritis (JIA). Apparently, no significant increase in opportunistic infections, malignancies or deaths has been observed even with a follow-up period of 8 years [67-69]. In addition, long-term safety using etanercept for childhood psoriasis is also reported in a larger study evaluating adverse events after 96 weeks, and in a single-case report with a follow-up of 38 months [64,70]. In conclusion, LOE of using etanercept in the treatment of psoriasis in children older than 6 years is judged as 1b.

Adalimumab

This fully human monoclonal antibody to TNF-α has been approved and used in children >4 years of age for the treatment of JIA [50,71] and recently also been approved for the treatment of severe chronic plaque psoriasis in children based on a randomized, double-blinded study [19].

The literature search produced two case reports describing the treatment of recalcitrant adolescent psoriasis with adalimumab. One case presented a 17-year-old girl with GPP who received 40 mg subcutaneous injection every other week while treated with mtx 20 mg/week and 400 mg/day cyclosporine. With this treatment regimen, the patient reported a dramatic improvement in her joint symptoms within 24 hours. A few days later, improvement was noticed in her psoriasis. Two months after beginning adalimumab therapy, almost complete resolution of her psoriatic lesions was observed. Five months after initiating adalimumab, mtx was discontinued and cyclosporine reduced to 100 mg daily and subsequently stopped [72]. The other case presented a 13-year-old girl with erythrodermic and pustular psoriasis responding neither to infliximab nor to etanercept. She was treated with adalimumab 40 mg/week 0 and 1 and then every other week thereafter. After eight weeks of treatment, a great improvement was achieved with a reduction of more than 90% in BSA and a PASI response of 1.8(initial PASI score not reported). After 16 weeks of treatment, the patient remained in complete remission [73]. A randomized, double-blinded study comparing adalimumab with mtx in patients between 4-17 years of age with plaque type psoriasis was completed in December 2014 and adalimumab was FDA approved in Marts 2015 for severe chronic plaque psoriasis in children >4 years if topical or phototherapy are not tolerated nor effective [19]. LOE is judged as level 1b.

Infliximab

Infliximab is a chimeric mouse/human monoclonal antibody that binds with high affinity and specificity to TNFα and neutralises its biologic activity. Infliximab has been reported to provide a rapid and significant clinical effect when administered as monotherapy to adult patients with moderate to severe psoriasis [74]. The literature search revealed five case reports concerning treatment of childhood psoriasis with infliximab, all reporting treatment to be successful [65,66,75,76,77]. However, several studies present children with inflammatory bowel disease treated with infliximab who develop psoriasis-like skin affection as an adverse event [78-80]. Infliximab infusions were given at a dosage of 3.3 to 5 mg/kg. Infusion intervals varied, but infusions were predominantly administered at week 0, 2, and 6, and every 7 or 8 weeks thereafter. Treatment duration of up to 30 months was described. No adverse events were described [65,66,75,76]. One patient, who was treated for 1 year, had to stop treatment due to loss of effect after 10 months of treatment and was switched to etanercept [66]. Another patient was switched from etanercept to infliximab [65]. In one patient with both psoriatic arthritis and linear and guttate psoriasis, the skin lesions were less responsive to treatment than the arthritis [75]. No double-blinded, placebo-controlled trials have been conducted, and the LOE of using infliximab in children with psoriasis can only be judged as level 5.

Ustekinumab

Ustekinumab is a human monoclonal antibody that targets the shared p40 subunit of interleukin-12 and -23 (IL-12, IL-23), preventing binding to their receptors on T-cells and natural-killer cells. This agent is approved for the treatment of moderate to severe psoriasis vulgaris in adults and has recently been approved in adolescent. It is administered as a subcutaneous injection at treatment start, at week 4 and then every 12 weeks [50].

To date, three published case reports describe the use of ustekinumab in adolescents. One case is a 14-year-old male with plaque type psoriasis. At week 16, the PASI reduction was 90%, and after 1 year he had cleared his symptoms [81]. Another patient was a 16-year-old male, with an initial PASI of 21.2 and a body weight of 145 kg. He was commenced on 90mg at week 0 and 4 and then every 12th weeks. At week 8, he had complete clearance of his psoriasis with a PASI score of 0, which he maintained for a minimum of 18 months. He had no side effects and lost 10 kg body weight [82]. Final case reports of a 12-year-old male with severe plaque psoriasis who gained a rapid excellent sustained response achieving PASI and DLQI at zero after 8 weeks [83]. The regime was as described in previous cases. A multicentre randomized, double-blinded, placebo-controlled trial evaluating the efficacy and safety of ustekinumab in the treatment of adolescent patients aged 12 to 17 years with moderate to severe plaque psoriasis has just been completed. 110 patients were included and assigned to standard dose of 0.75 mg/kg or half-standard dose or placebo. Ustekinumab was significantly superior compared with placebo [84]. LOE is judged as level 1b.

Discussion

Current conclusions and treatment algorithms on the treatment of childhood psoriasis are based on studies with low LOE. Furthermore, when choosing the best treatment option for the individual patient, several other issues must be taken into consideration e.g. age; type and severity of psoriasis; costs; practicality; side effects and comorbidities.

Mtx is presented as the conventional first-line of systemic treatment of psoriasis in children [85,86]. However, no double-blinded, placebo-controlled trials have been conducted, but recently it has been investigated head-to-neck against adalimumab. Adalimumab demonstrated significantly improvement in PASI 75 compared with mtx. But the difference in PGA was only a strong tendency [19]. Currently etanercept and recently adalimumab and ustekinumab are the only systemic drugs approved for psoriasis vulgaris in children aged below 18 years. Etanercept is the biologic agent on which most evidence for its efficacy and safety as a treatment of childhood psoriasis has been accumulated [6,50]. Etanercept has therefore been approved by the FDA and the EMA for use in children from six years of age. Furthermore, the long-term safety data on the use of etanercept for childhood psoriasis has also been reported [64,70]. Recently, in 2015, adalimumab was approved for use in severe childhood psoriasis from four years of age and without the restriction that mtx was ineffective or not tolerated. Additionally in 2015, Ustekinumab gained approval for the treatment in adolescence (>12 years) with moderate-severe psoriasis.

Thus, a wider range of systemic treatment options is becoming available. However, further studies, preferably randomized, double-blinded long-term head-to-neck controlled trials, are highly needed for the establishment of evidence-based guidelines for systemic treatment of childhood psoriasis.

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Conflict of Interest

L.I. has served as a consultant and/or paid speaker for, and/or participated in clinical trials sponsored by, AbbVie, Almirall, Amgen, Celgene, Centocor, Eli Lilly, Janssen-Cilag, LEO Pharma, MSD, Novartis, Pfizer and UCB. T.B. has participated in courses and/ or congresses sponsored by AbbVie, Janssen-Cilag, LEO Pharma, Novartis and Pfizer. Current PhD study is partly financed by Novartis.

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