

Can Influenced Choices be Consented? A Qualitative Study Involving Patients with Severe Uncontrolled Asthma Participating to Clinical Trials

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Abstract

Objective

Severe asthma is a difficult condition to treat; high-dose corticoids may ultimately represent a risk for patients and are not always enough to relieve them. Some find they in a therapeutic dead-end and have no other perspective than a clinical trial to help them to acquire a better quality of life and no long fearing a life-threatening exacerbation.

With such a strong influence in their decision, was it still consent or a coerced choice?

Methods

The study used a qualitative descriptive design consisting of 20 face-to-face interviews of patients with severe uncontrolled asthma who have consent to clinical trials in Marseille, France. Transcribed interviews were analyzed through thematic content analysis then discussed using philosophical tools.

Results

Two main themes have emerged: (1) the confusion between constraint and influence concerning the disease and the consent itself (2) the important role of the medical staff in the patient consent whom have a full confidence in their judgment. Patients are often confused when they talk about their decision making but when they think through, they feel like they had the choice and they were grateful to be able to participate. They also rely on their doctors to explain the forms instead of reading them, thus risking giving a not so informed consent.

Conclusion

Patients were performing voluntary actions in a context repressing their freedoms, but not annihilating it. They were not forced by others to integrate the protocol, they were influenced by the disease but they decided freely and voluntarily, so in this situation, influenced choices can be consented. However, relying only on doctors' intelligences instead of reading consent forms remain an ethical issue because of the potentially biased lightening it implies.

Keywords: Informed consent; Clinical trials; Patient perspective; Research ethics; Philosophy; Clinical ethics; Severe asthma; Uncontrolled asthma; Therapeutic dead-end.

Background

With the aging of the population, the modern lifestyle and contemporary scourges such as pollution, modern societies are confronted with a continuous increase of chronic diseases [1] and consequently the number of new therapeutics researches in the matter. Asthma is one of these pathologies directly resulting from these environmental upheavals and the severe ones are often uncontrolled [2] but many trials are in progress [3]. There are several forms of severe asthma, and all of them involve the burden of illness [4]; only few treatments, including corticoids, allow a stabilization of the disease.

But in severe uncontrolled asthma, those treatments prove to be ineffective and patients find themselves in a situation of therapeutic dead-end without incurring a vital urgency, but they may have greater risks of fatal exacerbation and their high medication increase the risk of steroid related adverse effects [5]. Some already have a treatment, but this one does not work fully and doses are sometimes so high they become an extra burden [6]. Clinical trials offered to these specific patients have the distinction of addressing people whose health is at risk, but who can continue to live despite a very poor quality of life. Many inquiries deal with informed consent in clinical research for patients with serious conditions such as cancer [7] but knowing the specificity of uncontrolled asthma, a disease which may involve jeopardy without involving a deadline, can we expect an informed consent in this peculiar situation? With cancer trials, patients are in a

therapeutic “dead-end” too sometimes and have to face an urgent situation which symbolizes a potential “deadline” if the trial doesn’t work [8]. Patients with severe uncontrolled asthma are not in imminent danger, but it is possible that they will have a life-threatening exacerbation [9] if they do not find an appropriate medication to their pathology. Clinical trials appear to be the only hope for new drugs. This specificity presents an ethical question not studied until then: when the danger is likely to come and the quality of life is already reduced, is consent to clinical trial a choice or does this influence become a constraint?

The informed consent was defined especially by Hewlett S: “Consent is an autonomous authorization by one person to permit another person to carry out an agreed procedure which affects the subject and therefore by asking patients to consent to research, we respect their wishes, enable them to be self-governing and uphold the principle of respect for persons” [10]. Consent must be autonomous and the result of a choice, yet the ethical issue of patient consent to participate in a research protocol as the only alternative are worth asking. More broadly, we can wonder if a person suffering from a chronic and disabling pathology, which represents a major influence, is free to choose to integrate a clinical trial.

Respect for the autonomy of clinical trial subjects has become a leitmotiv in recent decades [11]. Meanwhile, chronic diseases such as severe asthma impact patients in their quality of life by altering their autonomy, acting as an important influence [12]. Choices are the result of a context, like freedom, they exist in an environment [13], and our investigation aims to determine if this influence, uncontrolled disease, is compatible with an informed consent to clinical research. It is the aporia of freedom that is underpinned by these words, autonomy being its conceptual representation in medical ethics. If patients feel constrained by their pathologies, they may not have conceptually given a free consent upon integration, although they were not legally compelled.

Methods

Study design

We lead this study by conducting unique, semi-structured interviews lasting between 20 minutes and one hour. The interviews took place at the North Hospital, Marseille, France, in the mere presence of the patient and the leader of the investigation. Qualitative methods seemed more suited to this research because they really allow hearing the patient’s point of view, in its complexity, and that was the challenge of this work.

Study setting and population

The study was conducted from August 2017 to May 2018. The population selected for this study were 20 patients, twelve women and eight men between 45 and 75 years old. They were all in a therapeutic dead-end and included in a clinical trial for at least one year, so that they had a perspective on their integration into the trial and on their consent to it. Patients with severe asthma were selected, their disease being chronic and significantly impacting their quality of life without risking imminent danger [14]. They were not all included in the same clinical trials, but all were part of the Clinic of Bronchi, Allergy and Sleep of the North Hospital of Marseille, France. They were recruited at one of their monthly appointments, the pharmacist in charge of their file presented the qualitative survey and they had the time they wanted

to respond favorably or not. Only three patients refused the proposal because they did not have enough time for it. They will all remain anonymous.

Analysis

The method of analysis selected for this research is the inductive one because we did not wish to elaborate hypothesis before carrying out our interviews, this in order to give the primacy to the investigation, to the observation and to the experience to establish a general rule if possible, using the “Grounded Theory” [15]. The interviews were recorded using an electronic device, fully transcribed by hand and analyzed through thematic content analysis [16], both vertically (on each interview) and horizontally (set of interviews).

Results

Confusion between constraints and influences

The main theme to have emerged is the confusion between constraints and influences. Philosophically, constraint is an obstacle encountered in the performance of an action, it is external to the agent (others mostly) and coercive, it forces the agent to perform an act contrary to his will [17]. The notion of influence refers to a mysterious power, effective because invisible, it can condition our behavior or impact our decisions [17]. Patients have difficulty expressing themselves on this subject, confusing the constraints created by the disease with the choice to integrate a clinical trial. But it is important to note the difference between a strong motivation to perform an action, and the modalities of the action itself, which was not done by many of them. Patient 1 said that there was “nothing else to do”, patient 12 said: “No, in this disease there is no choice. There is no choice to make. There is a choice in the end with cortisone, and God knows what cortisone does”. They all talk about their illness and the obligations it has brought, the changes it has forced and the role it’s had in their decision-making.

However, every patient expresses his desire to improve his health and to get out of this dead-end, a great majority continues by explaining having lived this integration like a choice, because one did not impose anything on them and that they had the choice between to get in the clinical trial or not. Concerning the pathology’s specificity, this decision is somehow seen as a chance given the hardships experienced, an opportunity to cope, as expressed by Patient 8: “I was lucky to have had this choice. “. Patient 14 continued by saying: “A choice ... Yes and no. Because we do not have choice when we are sick. Of course I had the choice to do it or not”. These decisions are complex, integrating the trial represents a high risk, as does failure to act. Other patients argue that whatever happens, they always have the choice, as patient 18 said: “We always have a choice. Even if we are in a situation of therapeutic dead-end, we have the choice anyway. But, we’re still a bit stuck. When drugs doesn’t help anymore (...). But we still have the choice. We can say yes or no. I could go on like this too. “. This patient felt lucky too, and pragmatically argued that no one forced him, so this was his choice.

The theme of risk was also naturally addressed by all patients, as patient 9 who said: “It is a free choice. There is still this possibility of going out at any time, so somewhere; it is a kind of calculated risk. “. Because they were already at risk by being sick, then the calculation was already biased as patients stated, their health were threatened and

this was an opportunity for them, they choose to take the risk rather than to think about it.

The important role of the medical staff

Most of them chose to ask a few questions, the patient 13 said that the search for information was not so necessary: "I gave a look and I signed ... I trust them ". The question of trust in the medical profession was one of the main themes that emerged, as stated by patient 16: "This is where trust is important. It is to say that they are people I trust, in the hands of people I trust and who are not going to do anything wrong". Some people have immense gratitude to this medical team, expressed with the terms "Pride", "privilege", "recognition", "a chance", "I think it's great that they took me!", this appears to be linked with their situation of therapeutic dead-end because when they felt blocked, the medical staff showed them a way out so they feel grateful and trustful.

Twelve patients said they had read the forms, compared with 8 who said they did not. Many of them found it very redundant, Patient 5 also claimed not to have understood everything and needed the lighting of the doctors: "Because there are technical terms that you do not understand so you ask questions, (...) and they answered me as I wished", patients willingly rely on the team rather than these obscure forms as they call them. The informed dimension of consent appear as an issue because if they do not read intelligences about the trial and get advices only from the doctors, they took the risk of being directly influenced in their decision by them, or to do things they don't want to only because they did not know all the implications of this trial.

The theme of responsibility and commitment has come to explain that this balances the relationship, as the patient 9 said: "Psychologically, I think it's important to have this document. Because it's kind of a commitment from a team to make sure you get better. (...) I think it balances the relationship a bit. I find it good ". The patient is committed to respect certain things and not do others, they feel it as a membership rather than a contract and were reassured of this sharing.

Discussion

Philosophically, it is the question of choice that is relevant since they claim to have had the choice, and not really have it at the same time. This point of view was already expounded by Aristotle, he explained choices that seem involuntary: "Something of the sort happens also with regard to the throwing of goods overboard in a storm; for in the abstract no one throws goods away voluntarily; but on condition of its securing the safety of himself and his crew any sensible man does so", [18, 1110a5-20]. Some decisions seem to be the result of the constraint, however, the sailors in question had the possibility of not throwing their goods overboard, they only decided smartly under unfortunates circumstances, nobody would indeed take such a decision as an end in itself. Those decisions are complex, they represent a high risk as well as the fact of not acting and they question the difference between voluntary and involuntary actions. Some voluntary actions, as here, seem to be involuntary but are not, they are voluntary decisions made under strong influences, so this is about influence and not constraint here because they could have not done it. An involuntary action was presented by Aristotle as an action resulting from coercion or ignorance [18]. Patients here are not coerced, neither ignorant of their condition and terms of the deal (meanwhile they cannot know for sure all the drug effects, they know what the supposed risks are and they are aware that we cannot know more by now). We can ask ourselves if the

voluntary dimension of the action is sufficient to consider that it is free. The philosopher John Locke imagined an experiment of thought which presents itself in the following way: imagine a man carried in his sleep in a room where there is a person of his acquaintance, and unaware that the door is locked. He remains willingly in the room, but he cannot technically do otherwise (getting out [19]). This man seems to act voluntarily because he has remained willingly inside the room, but he is not aware of his confinement so he is unknowingly limited and if he knew, he would no longer feel free even if at this point, he feels so. The freedom of action appears as an illusory feeling in this thought experiment however determinations are, in fact, compatible with free decision if the subject is aware of them [20]. In the case of a clinical trial, the patient is aware of the disease influence on him, he knows that he is locked and the trial is an escape. He still has to make a decision knowing the specifics circumstances, he could stay or he could go. Patients feel the influence of the disease, but it is not a constraint concerning their inclusion in the protocol. They may not sign, they may even withdraw from the trial at any time without any justification, and with the very important influence that asthma exerts on their lives, the clinical trial becomes for them something that can restore the balance hurt by pathology, so this is an hopeful and desired way out. As Paul Appelbaum explained in his famous paper concerning voluntariness of consent to research: "The presence of influences does not mean that a decision is not voluntary. A decision is involuntary only if it is subject to a particular type of influence that is external, intentional, illegitimate, and causally linked to the choice of the research subject" [21]. Patients did not participate under constraint, technically, they were feeling the influence of the disease in their lives but they do not see themselves as guinea pigs, they are free to act on this proposal while they are in a world where they experience many constraints altering their quality of life [22]. Clinical consents are proposed by others, the patient can refuse or stop the trial at any time, which respects the principle of autonomy as the principle of beneficence [23] since a benefit is expected if the clinical trial is conclusive.

The other issue here being that the parts are not equal [24] the doctor has the knowledge which advantage him, and many patients feel diminished by the disease. According to Plato, friendship happens between two equal people, no matter their own characters, equity must be part of the equation [25]. Even if it's not specifically a friendship, it appears that they trust the team as they would trust a friend, they represent some kind of beneficent authority to them, and the consent contract appears to restore the delicate balance of the doctor / patient relationship. Patients feel favored by this agreement, they take it as a gift and deeply fear that it will stop, they see these clinical trials as a chance to get better, to get back to normal. The fact that medicine brings them a lot in this time of stress seems to increase the confidence they have in it, they rely on the service to heal them and the doctor to inform them, it is a delegation of skills. This reveals a delicate situation since consent is supposed to be free and informed, but if patients do not read the proposed documents to inform them, how can they be enlightened? How could we be sure they understand it all [26]? If they are informed only by doctors advices, they take the risk of partiality which may be a potentially biased lighting.

Conclusions

To conclude, this qualitative study has emerged that patients are confusing in their speech the terms constraint and influence. However, they are not forced to integrate the protocol, they are influenced by the

disease but they decide freely and voluntarily, so influenced choices can be consented but that depends on their conditions (no coercion what so ever and an hopeful and desired way out) and here, they were. Patients were performing voluntary actions in a context repressing their freedoms, but not annihilating it. Furthermore, an action is free according to the possibilities offered by its context, but also according to the voluntary nature of the action initiated by the agent and also depending on the impact of others on the said action. In the case of patients with uncontrolled asthma, they are not free to decide on their state of health, but they are free to integrate the clinical trial or not to do so, and this is the sole question of consent. They are certainly under the yoke of various influences, starting with the desire to live in the best possible way, however being aware of these determinations; they understand that this influence is independent of their wishes but that it has to be taken into account as a major argument in their decisions, which is still one.

The signing of forms is experienced as a formality, so the fact that 40% of interviewees did not read them reveals a major problem: the informed dimension of consent to research is not satisfactory, at least in theory because only relying to doctors as source of information raises the problem of bias. If the disease isn't a constraint and only stay a strong influence, doctors can be so, remembering that a constraint is when there is a coercion. Patients do not have doctor's knowledge, they are in bad health situation and they feel grateful to be in those clinical trials after years of uncontrolled asthma. If the doctor doesn't act according to an irreproachable code of ethics, he can influence the patient very easily in view of his position of superiority according to the particularly vulnerable situation of the patient. Likewise, in proposing the clinical trial, the doctor seems to restore the equilibrium the pathology has endangered. His role is primary, so he must be exemplary. The patient's consent to clinical research is fragile and inseparable from doctors ethics.

Declaration

Ethics approval and consent to participate

This enquiry was approved by the Ethics Committee of Aix-Marseille University, number 2017-14-06-004 . All patients who agreed to participate in the survey read and signed an information leaflet and consent.

Availability of data and material

Consents and notices are kept at the Espace de Réflexion Éthique PACA-Corse, Timone Adult Hospital, 264 rue Saint Pierre 13385 Marseille, France. All recordings, audio and transcribed, are also preserved. No other tools were used.

Competing Interests

The author declares to have no conflict of interests.

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Authors' Contributions

This research involved only one author who lead this study and analyze it on her own.

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